

MATTERS OTHER THAN MEDICINE

Bandolier has traditionally concentrated on examining systematic reviews and meta-analyses of clinical trials of treatments, and trying to make sense of them in ways that ordinary mortals like us can understand. But medical treatments are only one side of the coin of improved health and longevity. There's also the not insignificant factor of healthy, or unhealthy, living.

Speculation and precision

John Bunker [1] set out to try and estimate the contribution of medicine to improvements in life expectancy and quality of life since 1950. He himself says that any estimates of medicine's contribution to health can only be more than speculative and less than precise. The information he used came from several sources - changes in disease-specific death rates from the US National Center for Health Statistics and data on medical improvements from trials and meta-analyses.

Heart disease

In heart disease, for example, age adjusted death rates fell in the US from 307 to 156 per 100,000 between 1950 and 1989, about half of the fall in death rates for all causes. Over the same period overall life expectancy increased by 7.1 years, and so it was estimated that some 3.4 years of the improved life expectancy resulted from the fall in the death rate from heart disease.

Reviewing the evidence on the efficacy of medical interventions in heart disease, it was estimated that 40% of the decline in the death rate could be attributed to coronary care units, treatment of hypertension, and medical and surgical treatment of ischaemic heart disease. So 40% of the 3.4 years (1.4 years) could be attributed to medicine and health care.

Bottom line

The approach was extended to other areas, and the bottom line was an estimate that medical care can be credited with five of the 30 years of increased life expectancy in this century, and three of the seven years since 1950. A gain of five years of life expectancy is equivalent to halving the death rate at every age. Five years is equivalent to the loss in life expectancy due to smoking 20 cigarettes a day from age 20.

The contribution of medical care to the *quality* of life was also estimated. The number of years of poor quality life from severe chronic disease spared to individuals by medical care is estimated to be five years.

Tesco phenomenon

Other changes, social and economic, have had a big impact on improved length and quality. Improvements in transportation, agriculture and industrial processes mean that people have better education, have more money to spend, improved diets, annual holidays, sport and other leisure activities like cultivating the allotment.

In recent years, the advent of the supermarket means that better quality vegetables are more available, imported from around the world. So now we eat more vegetables all year round. Consumption of tomatoes in Britain is twice that of a few years ago. The result is that, on a population basis, antioxidant levels have increased, and that will have a beneficial effect on heart disease and cancer. Eating tomatoes and carrots, for instance, is thought each to reduce the risk of prostate cancer by about 30%.

Systematic reviews and meta-analyses of elements of healthy living are beginning to give us some idea of the weight of evidence for all sorts of lifestyle issues. Individuals can to an increasing extent control these for themselves, with diet and exercise being two of the most important. *Bandolier* will look for more of these. In this issue we examine Soya intake and its effects on lipids and menopausal symptoms, as one example. A bit touchy-feely, perhaps, but if we can put a hard edge to the touchy-feely bits of life, so much the better.

New Zealand

A welcome to the GPs in New Zealand who have started receiving *Bandolier* on a regular basis. For those of you who are electronic, there is a useful list of Internet addresses on page 5.

- 1 JP Bunker. Medicine matters after all. *J Roy Coll Phys (Lond)* 1995 29: 105-19.

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The views expressed in Bandolier are those of the authors, and are not necessarily those of the NHSE Anglia & Oxford

EVIDENCE-BASED EATING

Replacing animal protein with vegetable protein is one of those suggestions which is often encouraged, in part because eating less meat has been suggested to be reduce coronary heart disease risk. A meta-analysis examined the effects of soy protein intake on serum lipids [1], so that we can judge for ourselves what the benefits of dietary change may be for us.

Studies

Studies were selected for analysis if they had used isolated or textured soy protein, if they were controlled and had either a crossover design and if they provided baseline values so that the changes in each study group could be calculated. Excluded studies were those without a control group, those which used several sources of vegetable protein, and those which used whole soybeans rather than soy protein.

Twenty-nine articles had information from 38 clinical studies; 34 were in adults and four in children. Most studies used random assignment. Twenty used isolated soy protein, 15 textured soy protein and three used a combination of the two. All except one were designed to maintain weight and diets were predominantly those similar to Western diets in fat and cholesterol content. Soy protein intake averaged 47 g/day (range 17 to 124 g/day).

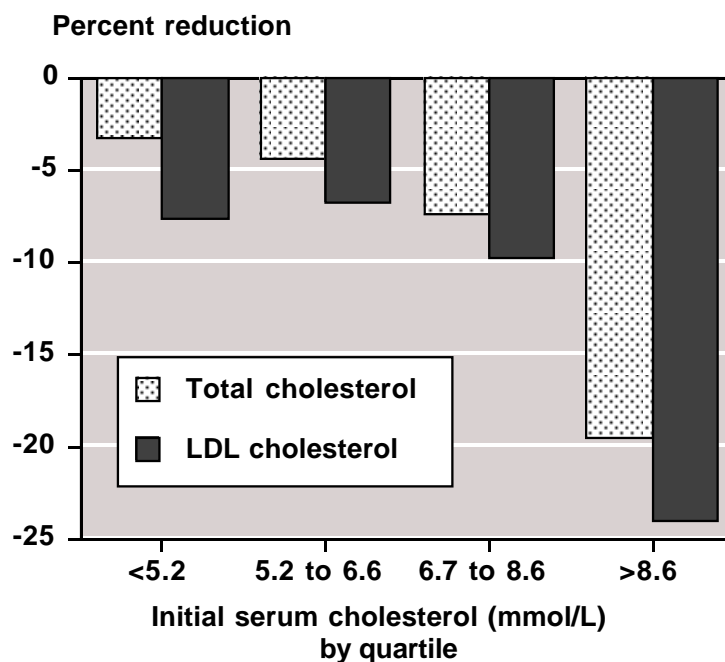
Results

There were significant reductions in total cholesterol, LDL cholesterol and serum triglycerides (Table below). The most important variable that predicted the extent of the reduction in serum cholesterol was the initial cholesterol level. The higher it was, the bigger the fall, as the depiction of results by quartiles shows (Figure). Significant falls occurred in the highest two quartiles of cholesterol, where the initial value was greater than 6.7 mmol/L.

Comment

The amounts of soy protein in single servings of various soy products is given in the box. It is clear, though, that benefits to health from reductions in serum lipids is most likely to accrue in those with high initial levels.

Effect of Soya in reducing serum cholesterol and LDL cholesterol by quartiles of initial cholesterol concentration



Reference:

- 1 JW Anderson, BM Johnstone, ME Cook-Newell. Meta-analysis of the effects of soy protein intake on serum lipids. New England Journal of Medicine 1995 333: 276-82.

Soy protein equivalents in various soy products

Soy product	Amount	Soy protein (g)
Soy milk	225 mL	4 to 10
Tofu	113 g	8 to 13
Soy flour	28 g	10 to 13
Isolated soy protein	28 g	23
Textured soy protein	113 g	11
Soy meat analogue	91 g	18

Mean change in serum lipids from baseline with soy diets

Variable	Number of studies	Number of subjects	Change mmol/L (95%CI)	Percent change
Total cholesterol	38	730	-0.60 (-0.35 to -0.85)	-9.3
LDL cholesterol	31	564	-0.56 (-0.30 to -0.82)	-12.9
HDL cholesterol	30	551	+0.03 (-0.08 to +0.14)	+2.4
VLDL cholesterol	20	255	-0.01 (-0.12 to +0.10)	-2.6
Triglycerides	30	628	-0.15 (-0.003 to -0.29)	-10.5

ALTERNATIVES FOR THE MENOPAUSE

There is a whole raft of reasons why women who suffer from menopausal symptoms do not wish to use hormone replacement therapy (HRT). These range from regarding the menopause as a natural transition, to thinking that osteoporosis or cardiovascular disease is not a threat to them individually, from an unwillingness to tolerate effects like breast tenderness or cyclical vaginal bleeding, to fear of cancer. It has been regularly remarked that only a small proportion of those women for whom HRT may be appropriate actually seek treatment, or accept it for long. Many women seek alternative, or "natural" remedies. A new review has examined the scientific and lay literature for evidence regarding the evidence that these alternative remedies have any effect [1].

Search

There was a broad and extensive search using several databases, including a consumer database in Toronto. A number of alternative remedies were included, ranging from nutritional supplements, herbal remedies, homeopathy and physical approaches.

Results

For all but one remedy there was no convincing evidence, or no evidence at all. Those for which there was no evidence in the form of randomised placebo-controlled studies included any herbal remedy, homeopathy, chiropractic, massage, exercise, acupuncture or relaxation techniques. Food supplements like vitamin E and evening primrose oil were found to have no benefit over placebo.

But there was a story to be told for phytoestrogens, like those from Soya:

- ◆ A randomised, double-blind study comparing daily supplements of 45 g soy flour with 45 g wheat flour found a more rapid and continuous reduction of 40% in hot flushes with soy flour compared with wheat flour (25%).
- ◆ Japanese women, in whom the menopause is often without the hot flushes and other menopausal symptoms experienced by their western sisters, excrete up to 1000 times the amount of isoflavenoid oestrogens in their urine.
- ◆ Biological effects of phytoestrogens (perhaps with only 2% the potency of human oestrogens) are likely to be greater in postmenopausal women when oestrogen receptors may not be occupied.
- ◆ Some phytoestrogens have been found to have bone-sparing effects in experimental animals and in some human subjects.

A hill of beans?

So does the evidence for phytoestrogens in Soya amount to more than a hill of beans? Certainly it is less than the quantity of evidence we might normally expect - large randomised trials, for example. But there is a story being told, with some biological plausibility and some epidemiological and clinical evidence. Most importantly, women who may wish to consider alternative treatments for menopausal symptoms

know that someone has taken the time and trouble to sort out the best evidence available for them. Isoflavenoids extracted from Soya are now available in capsule form, to be used either as an alternative to eating large amounts of soya, or as a way of enhancing diets which already have some Soya content.

Reference:

- 1 MM Seidl, DE Stewart. Alternative treatments for menopausal symptoms. Systematic review of scientific and lay literature. Canadian Family Physician 1998 44: 1299-1308.

MENOPAUSAL DECISIONS

Making decisions about whether or not to use hormone replacement therapy (HRT) will never be easy for women. In the immediate post-menopausal period some women may have tremendous problems with flushing and other symptoms, for which oestrogen replacement is efficacious. Yet the main benefits of oestrogens on bone and cardiovascular risks are long term, and have to be balanced against small increased risks of breast cancer associated with oestrogen use. It's all very complicated, and information available for women is variable, so a randomised trial which examined different ways of giving information [1] is interesting.

Study

This study of 165 women recruited women at least one year past the menopause by referrals, posters and radio and other announcements. They were randomised to getting information about HRT either by the use of an American College of Pathologists educational pamphlet describing the benefits, risks and side-effects of HRT or to a specially-designed decision aid. The decision aid comprised a 32-page illustrated booklet plus a 40 minute audio tape providing information about coronary heart disease, osteoporosis, endometrial and breast cancer in some detail, information about HRT regimens, and steps to assess a woman's own benefits and risk according to her individual risks for these factors. It was designed to take about 40 minutes, and be used by the woman at home. Randomisation was properly done, and included strategies to reduce influences from researchers during interviews. Data analysis was done by individuals blind to assignments.

Outcomes

A whole range of outcomes was used, including scales which measured decisional conflict, general knowledge about HRT benefits and risks, acceptability of the decision aids, and decisions about use of HRT. Realistic expectations were determined by whether the women made a sensible judgement approximating to their present or future risk of heart disease, breast cancer, or hip fracture.

Results

Women using the decision aid had significantly less conflict over making a decision, and more women using the decision aid had responses indicating no conflicts about their deci-

sion. The biggest difference was in the proportion of women having realistic expectations about the effects on HRT on their risks for coronary heart disease, risk fracture and breast cancer (Figure).

Despite an overall increase in knowledge about HRT and appreciation of the risk and benefits of HRT, there was no difference in the decisions women made. In both groups, 58% declined HRT, 15% accepted treatment, and 27% remained unsure.

Comment

Women liked the decision aid, and those who used it found it more acceptable and made better judgements about their own personal position. It reduced the number of women who underestimated their baseline risks of heart disease and overestimated their baseline risks of breast cancer and the benefits and risks of HRT. In that respect it was a valuable educational tool.

Perhaps there's the rub. It was an educational tool, and despite better education women may not change their attitudes to HRT. But choosing HRT is not a one-time, all-or-none decision. Women may reflect, or their circumstances may change, or new treatments like selective oestrogen receptor modulators may become available. Women knowledgeable about HRT may make different decisions in the future, and will certainly be more confident if they want to change their minds.

Reference:

1 A O'Connor, P Tugwell, GA Wells et al. Randomized trial of a portable, self-administered decision aid for postmenopausal women considering long-term preventive hormone therapy. Medical Decision Making 1998 18: 295-303.

REST EASY IN YOUR BEDS

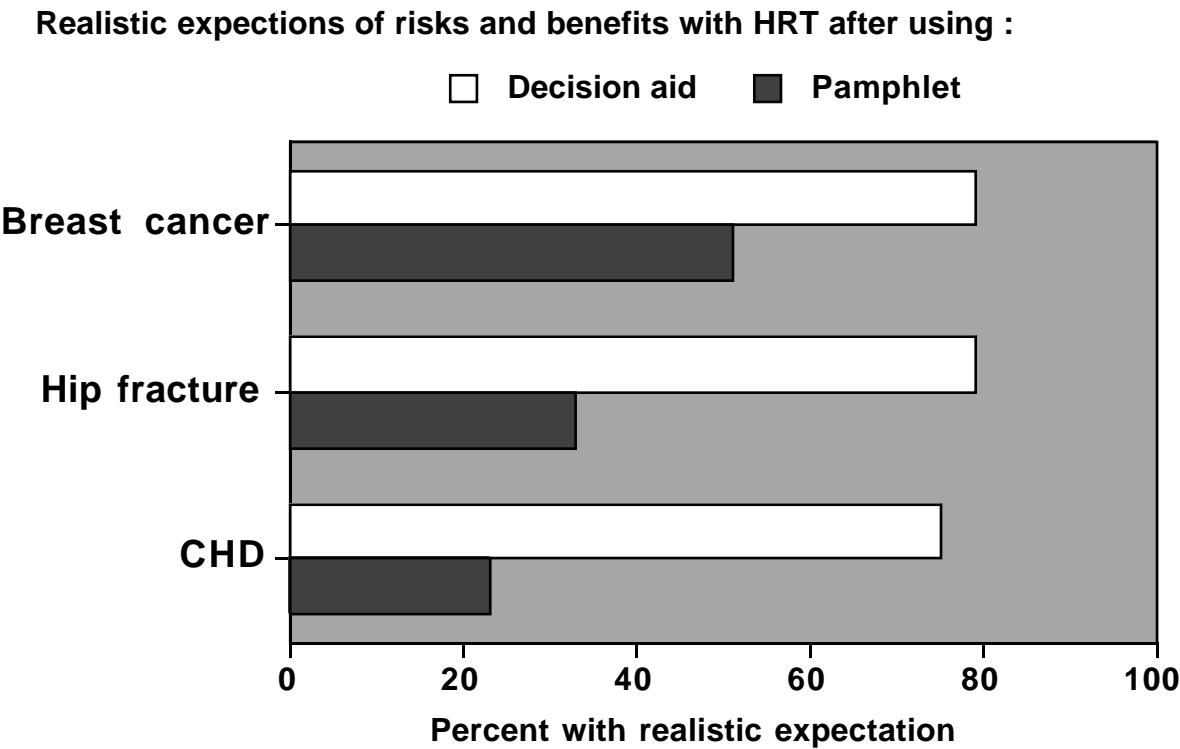
Numerous claims have been made about healthcare costs in the last year of life and the savings that could be made if only people would (or could) die easier and faster. A special article in the New England Journal of Medicine [1] helpfully addresses this issue by studying the "potential cost savings from legalising physician-assisted suicide".

Using information from the Dutch experience and Medicare and Medicaid costs in the USA the authors estimated the number of patients in the USA who might choose physician-assisted suicide and the cost savings that this would produce. The work is carefully done, and looks at how the figures they produce could be over- or under-estimates, and why.

The bottom line is that only small savings are likely to be realised were such a policy to be introduced. Savings, on a number of assumptions, amounted to no more than about 0.07% of total healthcare expenditure. The reasons for this, despite considerable hyperbole about the consumption of healthcare costs in the last month and year of life, include the fact that only 0.027% of people are likely to choose physician-assisted suicide in any one year. Put another way, that means that 99.97% of people would continue to receive usual health care at usual cost.

Reference:

1 EJ Emanuel, MP Battin. What are the potential cost savings from legalizing physician-assisted suicide? New England Journal of Medicine 1998 339: 167-172.



TIGHT UNDERPANTS

Sperm counts in the Western world are falling. Tight underpants? Oestrogens in water? Hormones in food? Desk-bound males? Stress? The “truth” of this observation has now achieved almost universal acceptance, and the issue has been transformed more into what is the cause and what can we do about it? We’ve even seen “projections” that by 2050, or 2150, or whatever, if sperm counts keep falling at the rate they are now, human reproduction will be entirely by cloning.

Studies

There’s a new analysis which questions this “truth” [1]. It revisits the data in an original meta-analysis [2] which collected 61 studies on sperm counts published between 1938 and 1990. Almost half of these studies (29/61) studied fewer than 50 men. The smallest number was nine and the largest 4435 men.

Originally a linear regression of the sperm count against year of the study showed a significant negative correlation. The new analysis [1] says that all the curve fitting done to date (several types have been tried) is wrong, and that if a flexible smoothing model is used then it shows that there may be a fall in the USA, but not in other countries.

Hang on a minute

Perplexed by all this, and getting more interested by the minute, *Bandolier* revisited the original data. Firstly, in the USA 80% of the total of 8416 men were studied after 1970. For the rest of the world it was 98%. So very little information exists before 1970. When we look at weighted mean values by decade or two (Table), all the data between 1970 and 1990 looks solid and reproducible, with no obvious changes going on. Only earlier information looks as if sperm counts were higher, but then in few men.

In the original meta-analysis considerable thought is given to possible sources of bias or analytical change to try to find possible origins for the change. They found none. Yet one sentence says that the coefficient of variation for determination of sperm density was 25 in an external quality check between ten German laboratories.

Let’s see what that means with a sperm count of, say, 70 million/mL. A coefficient of variation of 25% says that one standard deviation is 25% of 70, or about 18 million/mL. That means that 95% of results from these ten laboratories would be between plus two and minus two standard deviations, or between 34 and 106 million/mL. Yes, the highest and the lowest would vary by just about three-fold.

Close but no cigar!

Does the evidence we have constitute something to worry about? Is the story about falling sperm counts true? Readers can make their own minds up, but *Bandolier* isn’t going to lose sleep over this.

Reference:

- 1 S Becker, K Bihane. A meta-analysis of 61 sperm count studies revisited. *Fertility and Sterility* 1997 67: 1103-8.
- 2 E Carlsen, A Giwercman, N Keiding, NE Skakkebaek. Evidence for decreasing quality of semen during past 50 years. *British Medical Journal* 1992 305: 609-13.

Electronic evidence

New readers might like a short cut to some of the top UK electronic sites on evidence-based medicine on the Internet.

Bandolier:

<http://www.jr2.ox.ac.uk/Bandolier>

Centre for Evidence-based Medicine

<http://cebm.jr2.ox.ac.uk/>

The Cochrane Collaboration

<http://hiru.mcmaster.ca/COCHRANE/DEFAULT.HTM>

Development and Evaluation Services (DEC, plus reports)

<http://www.soton.ac.uk/~dec/>

Turning Research into Practice (TRIP searchable database)

<http://www.gwent.nhs.gov.uk/trip/>

Table: Sperm counts in USA and other countries from 1930 to 1990

Period	United States		Rest of the World	
	Number of men	Weighted mean sperm count (million/mL)	Number of men	Weighted mean sperm count (million/mL)
1930-1950	496	119	100	95
1951-1970	1184	107	0	no data
1971-1980	1868	72	427	73
1981-1990	4868	67	6004	77

PHYSIOTHERAPY AND SURGERY

Chest physiotherapy has been and sometimes is used to prevent and treat postoperative pulmonary complications, especially in high risk patients with a history of obesity, smoking, or old age, where lung function may be relatively impaired. Is it effective? A randomised trial of prophylactic chest physiotherapy from Sweden [1] comes to a very positive conclusion.

Trial

The study was conducted on all patients undergoing elective, open, upper abdominal surgery in one University hospital in Göteborg over a 14 month period. Randomisation was to physiotherapy being used or not used in alternate months. High risk patients were defined as those with age over 50 years who smoked, had a body mass index (BMI) of over 30 or who had a medical condition causing reduced lung function.

The intervention was a visit on the day before operation by a physiotherapist who trained the patient in breathing exercises with pursed lips, huffing and coughing hourly, information on changing position in bed, and the value of early mobilisation. High risk patients were additionally given a positive respiratory pressure mask for respiratory resistance training. Patients in the treatment group were told to take 30 deep breaths with huffing and coughing between every tenth breath every hour in daytime after the operation. After surgery physiotherapy continued, adjusted to pulmonary status.

In the control group, patients were given no preoperative training, and treatment by a physiotherapist occurred if a pulmonary complication developed.

Outcomes included surrogate measures like oxygen saturation, postoperative pulmonary complications, mobilisation and hospital stay. A pulmonary complication was defined as oxygen saturation less than 92%, or two of: temperature above 38.2°C, pathological lung sounds, radiological evidence of pneumonia or atelectasis.

Results

There were 174 patients given the prophylactic physiotherapy

and 192 in the control group. Groups were well matched for demographic variables and type of surgical procedure.

There were many fewer cases of pulmonary complications with prophylactic chest physiotherapy, for all patients where the number needed to treat (NNT) was 4.7, and for high and low risk patients, and obese patients, where the NNT was 2.1 (Table). There was a reduction in the number of patients with radiological and clinical pneumonia with treatment, where the NNT was 16.

There were significant increases in postoperative oxygen saturation with treatment, and for time to walking in the room and full mobilisation, but no difference in the length of hospital stay.

Comment

The good things about this study design were that it was comprehensive in its scope, including all patients over 14 months, and the pre-hoc identification of sub-groups for analysis. The alternate month randomisation was less than ideal because it raises the possibility of unconcealed allocation which is a known source of bias. The study was not blinded, but outcomes were objective and pre-defined.

This is good evidence that prophylactic physiotherapy reduces postoperative lung complications in people undergoing abdominal surgery. The effect may be greater in those at high risk, but not markedly so compared with those at low risk. Apart from people with BMI >30, there was overlap in the confidence intervals for the NNTs for pulmonary complications. Total hospital stay was not reduced, a fact not commented upon in the paper. But this is a blunt outcome, much affected by many other factors, and getting patients home earlier was not the focus of the study.

It would be interesting to have a health economist look at this. Would the costs of additional physiotherapy be outweighed by the costs of the complications prevented?

Reference:

- 1 M Fagevik Olsén, I Hahn, S Nordgren, H Lönroth, K Lundholm. Randomized controlled trial of prophylactic chest physiotherapy in major abdominal surgery. British Journal of Surgery 1997 84: 1535-38.

Effect of prophylactic chest physiotherapy on postoperative complications

Outcome	Patients	Treated	Control	NNT (95%CI)
Pulmonary complications	All	10/172	52/192	4.7 (3.5 to 7.1)
Pulmonary complications	Low risk	4/132	32/153	5.6 (4.0 to 9.3)
Pulmonary complications	High risk	6/40	20/39	2.8 (1.8 to 5.9)
Pulmonary complications	BMI >30	3/36	27/48	2.1 (1.6 to 3.2)
Pneumonia	All	1/172	13/192	16 (10 to 41)

ACUTE OTITIS MEDIA

Acute otitis media is a common reason for children being brought to their GP. Most children experience at least one episode by the time they are seven years old. Acute otitis media is one of the most common reasons for prescribing antibiotics, but the value of prescribing antibiotics is increasingly questioned, especially now with concerns about increasing antibiotic resistance.

Despite this, there are often pressures to prescribe antibiotics and reasons why such prescribing may be appropriate. One question which then arises is whether to go for a course of antibiotics over 10 days or so, or whether a short course of five days or less may be equally efficacious. A new meta-analysis of trials answers the question [1].

Review

A search sought randomised trials comparing different durations of antibiotic treatment in children with a diagnosis of acute otitis media. Searching was thorough, and process issues were well addressed. Thirty-two trials were found and included, including 17 with short-acting antibiotics (eg penicillin V potassium, amoxicillin), four with ceftriaxone sodium, and 11 with azithromycin.

Outcomes

The outcomes used were treatment failure at 8-19 days and at 20-30 days.

Results

The meta-analysis used Cochrane review methods, reporting odds ratios with no individual trial information, making it difficult to plot results or describe actual rates of success or failure, and *Bandolier* has a problem with odds ratios anyway. Summarising the main results, therefore:

- ◆ At 8-19 days, longer courses of antibiotics had a lower rate of treatment failure, with a difference in risk of 7.8%. Thus the number needed to treat to experience an additional failure with short-acting antibiotics was 13 (95% confidence interval 8.6 to 25). The odds ratio was significantly in favour of the longer course at 1.52 (95% confidence interval 1.17 to 1.98) using results from 1524 children analysed.
- ◆ At 20-30 days, longer courses of antibiotics also had a lower rate of treatment failure, but with a difference in risk of only 2.3%. Thus the number needed to treat to experience an additional failure with short-acting antibiotics was 43 (95% confidence interval 20 to no benefit). But there was no statistically significant difference, with an odds ratio of 1.22 (95% confidence interval 0.98 to 1.54) in results from 2115 children analysed.

Comment

This is a thorough review, with many sub-group and sensitivity analyses. None detract from the main findings, that

long courses of antibiotics confer little, if any, benefit over short courses. The fact that there is a benefit at 8-16 days is probably more of a reflection of the fact that the long course is only just completed and does not allow for any recurrence in the time.

Reference:

- 1 AL Kozyrskyi, GE Hildes-Ripstein, SE Longstaffe et al. Treatment of acute otitis media with a shortened course of antibiotics. JAMA 1998 279: 1736-42.

VOLUNTEERING

"Never volunteer for anything" is one of those old sayings that somehow gains credibility through repetition, though it may be one of those peculiarly British things. There may, though, be times when volunteering is a good thing. A (rather difficult) meta-analysis on the effects of volunteering on older volunteers and the people they serve suggests it may be a good idea.

Analysis

Using a wide searching strategy, 51 manuscripts were found, of which 37 had information that could be used to calculate effect sizes and were used for the analysis. Thirty had information about the effects of volunteering on older people, and ten on the people they serve. Most studies were performed in the USA. These were not randomised trials in the main, but most used standardised outcome measures measuring life satisfaction or happiness. Direct helping was the most common form of volunteering, with some using indirect helping or membership of groups.

The statistical analysis in this study was complicated. Ultimately it used a statistic called Cohen's *U3*. For example, a *U3* of 0.75 comparing a group of volunteers with their non-volunteering counterparts on life satisfaction would be simply interpretable as 75% of the volunteers scoring higher on a measure of life satisfaction score than their average non-volunteering counterpart.

Results

The number of older volunteers studied varied from 15 to 2164 (median 98), with an average age of about 70 years, and a predominance of white, female and unmarried (predominately widowed) people. People served ranged from 54 to 739 participants in each study (median 70), with little demographic detail about them.

Older volunteers

The study concluded that 70% of older volunteers enjoy a greater quality of life than the average non-volunteer does. Active volunteer participation seemed to be better than a passive voluntary membership or engagement in some form of activity.

People served

The study concluded that 85% of people served by older volunteers enjoy a greater quality of life than the average person

in a comparison group. Examples would be nursing home residents being less depressed when visited and helped by volunteers.

Comment

It seems that both older volunteers and the people they serve benefit most from the experience when it involves a face-to-face helping relationship. Most healthier older people are not in paid employment, but they represent a huge human resource, certainly able and perhaps willing to help both themselves and others.

Examples of programmes in the USA include a Retired Senior Volunteers Program (RSVP) in which volunteers serve vulnerable older people, and a foster grandparents programme, which speaks for itself.

This is a complicated review, and without getting and reading all the papers it is almost impossible adequately to assess its quality. Randomised trials there may not be, but despite this the review shows what has been done (mainly in the USA), identifies the literature, and may give clues as to what would constitute a meaningful study. Most of all it gives the idea, the hope, perhaps, that there are things that could (and perhaps should) be done given some spark and a few resources.

Reference:

- 1 JA Wheeler, KM Gorey, B Greenblatt. The beneficial effects of volunteering for older volunteers and the people they serve: a meta-analysis. *International Journal of Aging and Human Development* 1998 47: 69-79.

MINDSTRETCHER

From time-to-time questions are asked about why meta-analyses and randomised trials do not always agree. *Bandolier* found itself scratching its head about why this seemed to be the case regarding two recent publications, one a meta-analysis [1] which concluded that nonoxynol-9 prevented sexually transmitted infections, and a randomised trial [2] which concluded the opposite.

Background

Nonoxynol-9 is a nonionic detergent that works as a spermicide by disrupting the membranes of epithelial and sperm cells. It has been seen to do much the same to sexually transmitted pathogens in the test tube, including viruses like Herpes simplex and HIV.

Meta-analysis

The meta-analysis [1] looked for all trials and cohort, case-control or cross-sectional information. Included studies had to have original data to allow calculation of relative risks and spermicides containing nonoxynol-9 had to be used separately from other barrier contraceptive methods.

Twelve articles were identified. For six randomised trials looking at gonorrhoea (1881 women) the relative risk of trans-

mission was 0.62 (95% confidence interval 0.49 to 0.78). Four randomised trials evaluating Chlamydial infection had a relative risk of 0.75 (0.62 to 0.91). There was insufficient information for HIV.

So clearly nonoxynol-9 spermicides reduced transmission of sexually transmitted infections by 30-40% in randomised trials (confirmed by observational studies). Almost all were conducted among sex workers or health clinics with high rates of sexually transmitted infection.

Randomised trial

This was conducted in female sex workers in Cameroon. It was beautifully designed and conducted, and women (1170) were randomised to use of nonoxynol-9 film plus male condoms or placebo film plus condom for 12 months with monthly check ups and data collection. DNA probes were used to test for sexually transmitted infections.

At the end of the one-year trial there was no difference in infection rates for gonorrhoea, Chlamydia or HIV.

Spot the difference?

So why the big difference, and which was right? The eagle-eyed of you will have seen that the meta-analysis excluded barrier contraceptives (that is, it was testing the theory that nonoxynol-9 reduced sexually transmitted infections). The randomised trial positively encouraged (and monitored) use of condoms.

Chalk and cheese

There probably isn't any real controversy here. It's just that the meta-analysis and the randomised trial were testing different hypotheses in different circumstances. Why should the results be the same?

References:

- 1 RL Cook, MJ Rosenberg. Do spermicides containing nonoxynol-9 prevent sexually transmitted infections: A meta-analysis. *Sexually Transmitted Diseases* 1998 25: 144-50.
- 2 RE Roddy, L Zekeng, KA Ryan et al. A controlled trial of nonoxynol 9 film to reduce male-to-female transmission of sexually transmitted diseases. *New England Journal of Medicine* 1998 339: 504-10.

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